UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/426,340	10/25/99	SANDAL T	5600.200-US

HM12/0130

STEVE T ZELSON ESQ
NOVO NORDISK OF NORTH AMERICA INC
405 LEXINGTON AVENUE
SUITE 6400
NEW YORK NY 10174-6400

EXAMINER	
JOHANNSEN, D	
ART UNIT	**PAPER NUMBER**
1655	9

DATE MAILED: 01/30/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/426,340	Sandal et al
Examiner	**Group Art Unit**
Diana Johannsen	1655

☒ Responsive to communication(s) filed on *Nov 13, 2000*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-19, 21-25, and 27* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-19, 21-25, and 27* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

FINAL ACTION

1. This action is in response to paper no. 8 filed November 13, 2000. Claims 20 and 26 have been canceled and claims 1-16, 19, 21-25 and 27 have been amended. Claims 1-19, 21-25, and 27 are now pending. The amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims. **This action is FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

THE FOLLOWING ARE NEW GROUNDS OF OBJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

3. Claims 2-4 and 13-16 are objected to because of the following informalities. In claim 2, the phrase "culturing in a medium contains a substrate" should be amended to recite, e.g., "culturing in a medium that contains a substrate" or "culturing in a medium containing a substrate". In claim 13, the term "riched" should be amended to recite "enriched". Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

4. Claims 21-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons stated below and in the Office action of paper no. 7.

Claims 21-24 are indefinite over the recitation of the limitation "the desired gene" in claim 21. There is insufficient antecedent basis for this limitation in the claims, as claim 21 does not previously refer to or recite a "desired gene". The response does not traverse the rejection. This rejection is maintained.

Claim 27 is indefinite over the recitation of the phrase "wherein the DNA is an enzyme which comprises....". It is unclear as to what is meant by this language, as this language suggests that the recited DNA is a protein. The response does not traverse the rejection. This rejection is maintained.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

Claims 21-24 are indefinite over the recitation of the phrases "method of selecting a DNA sequence encoding a polypeptide of interest" and "selecting the DNA sequence of interest" in claim 21. As was discussed in the Office action of paper no. 7 with respect to the language "method of selecting a DNA sequence of interest", etc., it is unclear as to what is meant by the language "selecting a DNA sequence". For example, does this language require, e.g., detection of a sequence, isolation of a molecule, etc.? Further, it is unclear as to whether this language might

encompass solely mental steps of "selecting" a sequence. Additionally, with respect to step d) of claim 21, it is unclear as to how a "DNA sequence of interest" would "result from the screening of step c)". Applicants amendments have not clarified what actions would be required to accomplish "selection". The claims should be amended so as to provide a clear and definite descriptions of the objective and required final process step of the claimed method.

Claims 21-24 are indefinite over the recitation of the phrase "the DNA sequence of interest" in claim 21, step d). As a result of applicants amendments to the claims, the claims now lack antecedent basis for this language.

Claim Rejections - 35 U.S.C. § 102

5. In view of the cancellation of claims 20 and 26, the rejection of these claims under 35 U.S.C. 102(b) as being clearly anticipated by Duvick et al (WO 96/06175 [2/1996]) is moot.

6. In view of the amendment of claims 1 and 21 to require an environmental pool of organisms "isolated from soil, animal dung, insect dung, insect gut, animal stomach, sea or lake water, waste water, sludge, or sediment", the rejection of these claims under 35 U.S.C. 102(b) as being clearly anticipated by Duvick et al (WO 96/06175 [2/1996]) is withdrawn.

Claim Rejections - 35 U.S.C. § 103

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

7. Claims 1-7, 13-19, 21-25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duvick et al (WO 96/06175 [2/1996]) in view of Sarkar and Upadhyay (Folia Microbiologica 38(1):29-32 [1993]).

Duvick et al teach methods for identifying organisms having a particular enzymatic activity (fumonisin degradation) by growing the organisms in media in which the enzyme substrate (fumonisin B1 or B2) is provided as the sole carbon source (p. 4-6, Example 1). The organisms employed in Duvick et al's methods are from "environmental pools" (e.g., seeds and stalks [see p. 4]). Duvick et al teach genomic libraries and disclose methods for preparing said genomic libraries from the nucleic acids of the microorganisms encoding the protein of interest (a fumonisin esterase) (p. 24-25). Furthermore, Duvick et al discloses screening libraries for genes encoding proteins having the ability to degrade a particular substrate (fumonisin), and disclose "selecting" such genes for further analysis (subcloning, sequencing, expression, etc.) (p. 25). Duvick et al do not teach or suggest the use in their methods of environmental pools of organisms isolated from the sources set forth in claims 1 and 21. Furthermore, Duvick et al do not teach employing their methods to prepare libraries enriched in nucleic acids encoding a polypeptide "with an activity of interest" that acts on the substrates set forth in claim 4, and/or nucleic acids encoding enzymes of the types set forth in claims 16 or 27. Additionally, Duvick et al do not teach or suggest "selecting" genes encoding such polypeptides, as required by claim 24. Finally, Duvick et al do not teach or suggest employing growth conditions or "restrictions" such as those set forth in claim 7.

Sarkar and Upadhyay disclose that *Bacillus thermoalcaliphilus* isolated from an "the soil of a termite" produces a cellulase that is most stable at pH 8.5-9.5 and optimally active at 70°C (see entire reference, especially p. 29-30). Sarkar and Upadhyay teach growth of this bacterium in media comprising cellulose at 60°C, pH 8.5 (p. 29). In view of the teachings of Sarkar and Upadhyay, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Duvick et al so as to have prepared from a termite soil sample a genomic library enriched for a *B. thermoalcaliphilus* gene encoding the thermostable cellulase taught by Sarkar and Upadhyay, and so as to have "selected" that gene for further analysis. An ordinary artisan would have been motivated to have made such a modification for the advantage of, e.g., rapidly isolating and sequencing the cellulase-encoding gene, rapidly preparing recombinant forms of the cellulase for additional study or use, etc. With respect to claim 4, it is further noted that Sarkar and Upadhyay disclose that cellulose is a substrate for cellulase, and teach growth of cellulase producing organisms in media comprising cellulose. With respect to claim 5, it is noted that Duvick et al teach enrichment of a pool of organism by the imposition of growth restrictions (growth in media in which the substrate of the desired enzyme is the sole carbon source). With further reference to claim 6, it is noted that it is a property of the growth restrictions employed by Duvick et al and Sarkar and Upadhyay that they "comprise pH and temperature". With respect to claim 7, it is further noted that it would have been *prima facie* obvious to one of ordinary skill in the art to have selected the growth conditions taught by Sarkar and Upadhyay for use in the method of Duvick et al in view of Sarkar and

Upadhyay in order to have assured optimal growth of the bacterium from which nucleic acids of interest were to be cloned, for the advantages of convenience and efficiency. With respect to claim 23, it is noted that Duvick et al disclose screening clones for an "active enzyme" ("their ability to degrade fumonisin" and selection of "colonies that degrade fumonisin" (p. 25)).

It is noted that, with respect to the rejection of claims 4, 7, 16, 24, and 27 as being unpatentable over Duvick et al in view of Sarkar and Upadhyay in the Office action of paper no. 7, the response argues that Sarkar and Upadhyay fail to "cure the defects" of Duvick et al. The response further argues that the instant invention as compared to Duvick et al "avoids several time consuming and labor intensive steps because the instant invention is not concerned with the source of the gene encoding the activity of interest, and thus does not entail isolation of a strain". These arguments have been thoroughly considered but are not convincing. As the present claims recite the open transitional language "comprising", methods encompassed by the claims include not just methods limited to the particular steps recited therein, but methods including any number of additional steps. Further, the claims encompass the use of any types of steps necessary to accomplish, e.g., preparation of a gene library, screening, selection, etc. It is further noted that the Sarkar and Upadhyay reference has not been cited for its teachings related to any "defects" asserted by Applicant, but for its teachings of particular sample types, growth conditions, and enzyme activities, as set forth above.

8. Claims 1-9, 13-19, 21-25, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duvick et al in view of Cotta (Appl. Environment. Microbiol. 54(3):772-776 [3/1988]).

Duvick et al teach methods for identifying organisms having a particular enzymatic activity (fumonisin degradation) by growing the organisms in media in which the enzyme substrate (fumonisin B1 or B2) is provided as the sole carbon source (p. 4-6, Example 1). The organisms employed in Duvick et al's methods are from "environmental pools" (e.g., seeds and stalks [see p. 4]). Duvick et al teach genomic libraries and disclose methods for preparing said genomic libraries from the nucleic acids of the microorganisms encoding the protein of interest (a fumonisin esterase) (p. 24-25). Furthermore, Duvick et al discloses screening libraries for genes encoding proteins having the ability to degrade a particular substrate (fumonisin), and disclose "selecting" such genes for further analysis (subcloning, sequencing, expression, etc.) (p. 25). Duvick et al do not teach or suggest the use in their methods of environmental pools of organisms isolated from the sources set forth in claims 1 and 21. Particularly, Duvick et al do not teach or suggest employing their methods to prepare libraries enriched in nucleic acids encoding a polypeptide of interest from an environmental pool "isolated from an animal stomach or an insect gut", as required by claim 8, or from a pool of microorganisms "isolated from a cow's rumen", as required by claim 9. Further, Duvick et al do not teach employing their methods to prepare libraries enriched in nucleic acids encoding a polypeptide "with an activity of interest" that acts on the substrates set forth in claim 4, and/or nucleic acids encoding enzymes of the types set forth in

claims 16 or 27. Additionally, Duvick et al do not teach or suggest "selecting" genes encoding such polypeptides, as required by claim 24.

Cotta teaches that several bacteria present in the rumen of cattle produce amylases that degrade starch (see entire reference). In view of the teachings of Cotta, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Duvick et al so as to have prepared from a sample of bacteria isolated from cattle rumen genomic libraries enriched for genes encoding the amylases taught by Cotta, and so as to have "selected" such genes for further analysis. An ordinary artisan would have been motivated to have made such a modification for the advantage of, e.g., rapidly isolating and sequencing the amylase-encoding genes, rapidly preparing recombinant forms of the amylases for additional study or use, etc. With respect to claim 4, it is further noted that Cotta teaches that amylases degrade amylose (see, e.g., p. 773).

It is noted that, with respect to the rejection of claims 4, 8-9, 16, 24, and 27 as being unpatentable over Duvick et al in view of Cotta in the Office action of paper no. 7, the response argues that Cotta fails to "cure the defects" of Duvick et al, stating that "Knowledge that there are several bacteria in the presence of the rumen of cattle fails to provide instructions as to which of Duvick et al. selection/isolation/screening steps could be dispensed with". The response further argues that the instant invention as compared to Duvick et al "avoids several time consuming and labor intensive steps because the instant invention is not concerned with the source of the gene encoding the activity of interest, and thus does not entail isolation of a strain".

These arguments have been thoroughly considered but are not convincing. As the present claims recite the open transitional language "comprising", methods encompassed by the claims include not just methods limited to the particular steps recited therein, but methods including any number of additional steps. Further, the claims encompass the use of any types of steps necessary to accomplish, e.g., preparation of a gene library, screening, selection, etc. It is further noted that the Cotta reference has not been cited for its teachings related to any "defects" asserted by Applicant, but for its teachings of particular sample types and enzyme activities, as set forth above.

9. Claims 1- 8, 10, 12-19, 21-25, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duvick et al in view of Jacobsen and Schlein (J. Euk. Microbiol. 44(3):216-219 [1997]).

Duvick et al teach methods for identifying organisms having a particular enzymatic activity (fumonisin degradation) by growing the organisms in media in which the enzyme substrate (fumonisin B1 or B2) is provided as the sole carbon source (p. 4-6, Example 1). The organisms employed in Duvick et al's methods are from "environmental pools" (e.g., seeds and stalks [see p. 4]). Duvick et al teach genomic libraries and disclose methods for preparing said genomic libraries from the nucleic acids of the microorganisms encoding the protein of interest (a fumonisin esterase) (p. 24-25). Furthermore, Duvick et al discloses screening libraries for genes encoding proteins having the ability to degrade a particular substrate (fumonisin), and disclose "selecting" such genes for further analysis (subcloning, sequencing, expression, etc.) (p. 25).

Duvick et al do not teach or suggest the use in their methods of environmental pools of organisms isolated from the sources set forth in claims 1 and 21. Particularly, Duvick et al do not teach or suggest employing their methods to prepare libraries enriched in nucleic acids encoding a polypeptide of interest from an environmental pool "isolated from an animal stomach or an insect gut", as required by claim 8, or from "the gut of an insect of the *Isoptera, Lepidoptera, Coleoptera,* or *Diptera* families", as required by claim 10. Further, Duvick et al do not teach employing their methods to prepare libraries enriched in nucleic acids encoding a polypeptide "with an activity of interest" that acts on the substrates set forth in claim 4, and/or nucleic acids encoding enzymes of the types set forth in claims 16 or 27. With respect to claim 12, Duvick et al do not teach or suggest supplying a substrate in the feed of an animal or insect. Additionally, Duvick et al do not teach or suggest "selecting" genes encoding such polypeptides, as required by claim 24.

Jacobsen and Schlein teach that *Leishmania* present in the midgut of the sandfly *Phlebotomus papatasi* produce cellulases that degrade cellulose (see entire reference). In view of the teachings of Jacobsen and Schlein, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Duvick et al so as to have prepared from a sample of *Leishmania* isolated from sandfly midgut genomic libraries enriched for genes encoding the cellulases taught by Jacobsen and Schlein and so as to have "selected" such genes for further analysis. An ordinary artisan would have been motivated to have made such a modification for the advantage of, e.g., rapidly isolating and sequencing the

cellulase-encoding genes, rapidly preparing recombinant forms of the cellulases for additional study or use, etc. With respect to claim 4, it is noted that Jacobsen and Schlein teaches that cellulases degrade cellulose (see, e.g., p. 216). With respect to claim 10, it is noted that *Phlebotomus papatasi* is a member of the order *Diptera*. With respect to claim 12, it is noted that Jacobsen and Schlein suggest feeding flies with feed that comprises cellulose (p. 216).

It is noted that, with respect to the rejection of claims 4, 8, 10, 12, 16, 24, and 27 as being unpatentable over Duvick et al in view of Jacobsen and Schlein in the Office action of paper no. 7, the response argues that Jacobsen and Schlein fail to "cure the defects" of Duvick et al, stating that "Knowledge that 'Leishmania present in the midgut of the sandfly phlebotomus papatasi produce cellulases' fails to provide instructions as to which of Duvick et al. selection/isolation/screening steps could be dispensed with". The response further argues that the instant invention as compared to Duvick et al "avoids several time consuming and labor intensive steps because the instant invention is not concerned with the source of the gene encoding the activity of interest, and thus does not entail isolation of a strain". These arguments have been thoroughly considered but are not convincing. As the present claims recite the open transitional language "comprising", methods encompassed by the claims include not just methods limited to the particular steps recited therein, but methods including any number of additional steps. Further, the claims encompass the use of any types of steps necessary to accomplish, e.g., preparation of a gene library, screening, selection, etc. It is further noted that the Jacobsen and Schlein reference has not been cited for its teachings related to any "defects" asserted by

Applicant, but for its teachings of particular sample types and enzyme activities, as set forth above.

10. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Duvick et al in view of Jacobsen and Schlein, as applied to claims 1- 8, 10, 12-19, 21-25, and 27, above, and further in view of Siegle et al (US Patent No.4,027,037).

The combined references of Duvick et al and Jacobsen and Schlein do not teach or suggest preparing "enriched" gene libraries from microorganisms isolated from the guts of the insect species set forth in claim 11. It is noted that the instant claim is not limited to methods in which, e.g., a gene encoding a polypeptide having a particular activity in a particular species is identified or detected. Accordingly, the instant claim encompasses methods of preparing a library comprising any DNA "encoding a polypeptide with an activity of interest" from any pool of microorganisms isolated from the gut of any of the species set forth in the claim. Siegle et al teach a variety of orders and species of arthropods, including both *Phlebotomus* species and *Agrotis* species (col 6, line 32-col 7, line 38). In view of the teachings of Siegle et al, it would have been *prima facie* obvious at the time the invention was made to have modified the method of Duvick et al in view of Jacobsen and Schlein so as to have prepared enriched gene libraries from nucleic acids of the gut bacteria of any of the arthropods taught by Siegle et al, including *Agrotis* species. An ordinary artisan would have been motivated to have made such a modification for the advantage of, e.g., rapidly isolating and sequencing a gene encoding any polypeptide of interest, rapidly preparing recombinant forms such a polypeptide for additional study or use, etc.

It is noted that, with respect to the rejection of claim 11 as being unpatentable over Duvick et al in view of Jacobsen and Schlein and Siegle et al in the Office action of paper no. 7, the response argues that Jacobsen and Schlein, and Siegle et al, fail to "cure the defects" of Duvick et al, stating that "Knowledge that 'Leishmania present in the midgut of the sandfly phlebotomus papatasi produce cellulases'....combined with 'a variety of orders and species of arthropods'...fails to provide instructions as to which of Duvick et al. selection/isolation/screening steps could be dispensed with". The response further argues that the instant invention as compared to Duvick et al "avoids several time consuming and labor intensive steps because the instant invention is not concerned with the source of the gene encoding the activity of interest, and thus does not entail isolation of a strain". These arguments have been thoroughly considered but are not convincing. As the present claims recite the open transitional language "comprising", methods encompassed by the claims include not just methods limited to the particular steps recited therein, but methods including any number of additional steps. Further, the claims encompass the use of any types of steps necessary to accomplish, e.g., preparation of a gene library, screening, selection, etc. It is further noted that the Siegle et al reference has not been cited for its teachings related to any "defects" asserted by Applicant, but for its teachings of particular orders and species of arthropods, as set forth above.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday from 7:00 a.m. to 3:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at 703/308-1152. The fax phone number for the Technology Center where this application or proceeding is assigned is 703/305-3014 or 305-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana Johannsen

January 26, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1610

1/29/01